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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/801,292	03/15/2004	Yi-Chao Lee	5422-2	3057

27799 7590 04/24/2006

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EXAMINER	
GODDARD, LAURA B	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 04/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/801,292	LEE ET AL.	
	Examiner	Art Unit	
	Laura B. Goddard, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *8-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/7/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The Election filed February 15, 2006 in response to the Office Action of January 11, 2006 is acknowledged. Applicant elected Group I, claims 1-7 and the nucleic acid marker having SEQ ID NO:1. Because applicant did not state that the election was with traverse and did not distinctly and specifically point out any supposed errors in the restriction requirement, the restriction is maintained.

Claims 1-20 are pending. Claims 8-20 are withdrawn from further consideration by the examiner under 35 CFR 1.142(b) as being drawn to non-elected inventions. Claims 1-7, as drawn to a method of assessing whether a patient is afflicted with carcinoma comprising determining the amount of a nucleic acid marker SEQ ID NO:1 in a patient sample, are currently under prosecution.

Claim Objections

2. Claim 1 is objected to for containing subject material that is drawn to a non-elected invention. The claim recites "wherein the marker is selected from Table 1", Table 1 includes markers drawn to non-elected inventions. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for **a method of assessing whether a patient is afflicted with ovarian carcinoma, the method comprising a) determining the amount of SEQ ID NO:1 marker in a patient ovarian carcinoma tissue sample; b) determining the average normal amount of the SEQ ID NO:1 in a control non-cancerous ovarian tissue sample; and c) comparing the amounts of the marker between the patient ovarian carcinoma tissue sample and the control non-cancerous ovarian tissue sample, wherein a significant increase in the amount of the marker in the patient sample from the normal level is an indication that the patient is afflicted with ovarian carcinoma**, does not reasonably provide enablement for a method of assessing whether a patient is afflicted with carcinoma, the method comprising a) determining the amount of SEQ ID NO:1 marker in a patient sample; b) determining the normal amount of the SEQ ID NO:1 in a control non-cancerous sample; and c) comparing the amounts of the marker between the patient and the control sample, wherein a significant increase in the amount of the marker in the patient sample from the normal level is an indication that the patient is afflicted with carcinoma. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are drawn to a method of assessing whether a patient is afflicted with **carcinoma**, the method comprising a) determining the amount of SEQ ID NO:1 marker in a patient **sample**; b) determining the normal amount of the SEQ ID NO:1 in a control non-cancerous **sample**; and c) comparing the amounts of the marker between the patient and the control **sample**, wherein a significant increase in the amount of the marker in the patient **sample** from the normal level is an indication that the patient is afflicted with carcinoma. The claims are broadly drawn to a method of assessing

whether a patient is afflicted with **any** carcinoma comprising determining the amount of SEQ ID NO:1 marker in **any** sample taken from anywhere in the patient and comparing the level of marker to **any** control non-cancerous sample. Although claims 2 and 3 further limit the carcinoma being assessed, the claims do not indicate what sample is being tested for levels of SEQ ID NO:1.

The specification discloses SEQ ID NO:1 as a newly identified cancer therapeutic target that is overexpressed in carcinomas (p. 3). The specification discloses assessing the level of SEQ ID NO:1 nucleic acid in human normal ovary tissue and human ovary tumor tissue wherein the levels for SEQ ID NO:1 are measured by quantitative real-time PCR (qRT-PCR) and found to be up-regulated in ovarian cancer tissue (p. 14-17). The specification also discloses the up-regulation of SEQ ID NO:1 in cell lines listed on pages 13-14. A search of the prior and current art does not teach increased expression of SEQ ID NO:1 as indicative of cancer.

One cannot extrapolate the teaching of the specification to the scope of the claims because the specification only discloses measuring the amount of SEQ ID NO:1 in ovarian cancer tissue and comparing it to control ovarian tissue but does not provide guidance or examples of measuring levels of SEQ ID NO:1 in any other cancerous and normal tissues taken from a human. The specification does not provide examples of measuring levels of SEQ ID NO:1 in **both** carcinoma cell culture and its control cell counterpart, hence, one could not predictably determine what a "normal level" of SEQ ID NO:1 would be for comparison for the cell culture studies.

Further, even if the specification did demonstrate up-regulated expression of SEQ ID NO:1 in cell culture comparison studies, the art teaches that cell culture, particularly carcinoma cell lines, may not be representative of their *in vivo* counterparts. For example, Drexler et al (Leukemia and Lymphoma, 1993, 9:1-25) specifically teach, in the study of Hodgkin and Reed-Sternberg cancer cells in culture, that the acquisition or loss of certain properties during adaptation to culture systems cannot be excluded. This is exemplified by the teachings of Zellner et al (Clin. Can. Res., 1998, 4:1797-17802) who specifically teach that products are overexpressed in glioblastoma (GBM)-derived cell lines which are not overexpressed *in vivo*. Drexler et al further teach that only a few cell lines containing cells that resemble the *in vivo* cancer cells have been established and even for the bona fide cancer cell lines it in difficult to prove that the immortalized cells originated from a specific cancer cell (see abstract). Hsu (in Tissue Culture Methods and Applications, Kruse and Patterson, Eds, 1973, Academic Press, NY, see abstract, p.764) specifically teaches that it is well known that cell cultures in vitro frequently change their chromosomal constitutions (see abstract). It is clear that the unpredictability of using cancer cell lines is well known in the art since Slamon et al, (Cancer Cells, 1989, 7:371-384) specifically teach that for their studies they use clones from actual human tumor tissue because DNA in cell lines can acquire genetic changes *in vitro* that may not be representative of the gene *in vivo*, p. 373, col 1). Thus, based on the cell culture data presented in the specification, in the absence of data provided from primary tumor cells and normal controls, no one of skill in the art would believe it

more likely than not that the claimed method of assessing whether a patient is afflicted with **any** carcinoma would function as broadly claimed.

Finally, those of skill in the art recognize that a patient sample must be taken from the patient's cancerous tissue in order to detect and measure amounts of a nucleic acid marker that is indicative of the cancer. One of skill in the art could not predictably assess whether a patient is afflicted with carcinoma by determining the amount of a nucleic acid marker in a patient sample taken from **any** tissue or fluid other than the cancerous tissue itself and compare it to its non-cancerous counterpart. The specification does not provide guidance or examples of assessing whether a patient is afflicted with carcinoma using **any** sample from a patient other than ovarian carcinoma tissue and compared to non-cancerous ovarian tissue.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth, and it cannot be reasonably predicted assessing whether a patient is afflicted with carcinoma, will predictably function as claimed. Therefore, in view of the novel nature of the invention, what is unknown in the art because of the novel nature of the invention, the breadth of the claims, lack of guidance in the specification, and the absence of working examples, it would require undue experimentation for one skilled in the art to practice the invention as broadly claimed.

4. **Conclusion:** Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph but are free of the prior art. The closest prior art appears to be Beck et al (Gynecol Oncol, 1994, 53:196-201) and Strausberg et al (PNAS, 2002, 99:16899-16903). Beck et al

compare the expression of insulin receptors in ovarian cancer as compared to control normal ovarian tissue. Strausberg et al (see sequence search, GenEmbl, Result #1) identify SEQ ID NO:1 as a full-length human cDNA sequence. Beck et al and Strausberg et al do not teach or suggest a method of assessing whether a patient is afflicted with carcinoma or ovarian carcinoma comprising determining the amount of SEQ ID NO:1 in a patient sample and comparing the amount to a normal control.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura B. Goddard, Ph.D. whose telephone number is (571) 272-8788. The examiner can normally be reached on 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Laura B Goddard, Ph.D.
Examiner
Art Unit 1642

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER